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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/718,034

11/19/2003

Uri Herzberg

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EXAMINER

CLAYTOR, DEIRDRE RENEE

ART UNIT

PAPER NUMBER

1627

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/718,034	Applicant(s) HERZBERG ET AL.	
	Examiner Renee Claytor	Art Unit 1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 October 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6,25-57 and 59-71 is/are pending in the application.
- 4a) Of the above claim(s) 1-6,25-42,53-57 and 59 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 43-52, 60-71 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Arguments

It is noted that Applicants present arguments over the 35 USC 102(e) rejection over Kyle and the 35 USC 103 rejection over Bakthavatchalam; however, as Applicants have amended the claims to include compounds of Formula II, the rejections are withdrawn under 35 USC 102 and 35 USC 103 and the following new grounds of rejection are being made based on Applicants amendments.

Claim Rejections – 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-52, 60-66 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using ((6-trifluoromethyl-pyridin-3-yl)-[7-(3-trifluoromethyl-pyridin-2-yl)-quinazolin-4-yl]-amine, ([2-methyl-7-(3-trifluoromethyl-pyridin-2-yl)-quinazolin-4-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine to treat tolerance to morphine, does not reasonably provide enablement for using all of the various compounds of Formula II to inhibit the development of tolerance to an opioid narcotic analgesic. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApl's 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

1) The nature of the invention and the breadth of the claims: The nature of the invention and breadth of the claims is a method for inhibiting the development of tolerance to an opioid narcotic analgesic comprising continuously or repeatedly administering to a patient simultaneously or sequentially in either order; (i) an opioid narcotic analgesic and (ii) a tolerance-reducing amount of a nontoxic VR1 antagonist represented by the formula (II).

2) The state of the prior art: The state of the prior art regarding compounds with core structures that overlap with the current Formula II is taught in Meyer et al. (US Patent 4,621,082) which teaches renal vasodilating and diuretic action. The art does not teach a host of compounds of Formula II in treatment of diseases, and in particular for inhibiting the development of tolerance to an opioid analgesic.

3) The amount of direction or guidance presented: The specification teaches the use of particular VR1 antagonists in the treatment method of the instant claims. In particular, Example 12 teaches inhibition of the development of tolerance to morphine analgesia in rats using the VR1 antagonist ((6-trifluoromethyl-pyridin-3-yl)-[7-(3-trifluoromethyl-pyridin-2-yl)-quinazolin-4-yl]-amine and ([2-methyl-7-(3-trifluoromethyl-pyridin-2-yl)-quinazolin-4-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine which both showed an effect at treating tolerance to morphine analgesia. However, the results are not representative of all of the various possible formulations of Formula II. There are many possible substitutions of Ar₁, W, Y, Z, V, U, X and Ar₂ that will results in many different compounds of Formula II, of which there is no indication that every compound will be effective in the method.

4) The quantity of experimentation necessary: “A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed Cir. 1993)”. Undue experimentation would be required in order to practice Applicant's invention because there are no examples provided in the specification. One would have to determine a useful model that correlates with clinical efficacy, a dosage range would need to be determined as well as a route of administration. Further, if any of the above failed, then the artisan would have to start over again in an effort to determine the

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suitable methods, dosage ranges and routes of administration in which to determine if the compounds will work to treat the disorders listed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627